

* * * * *

=> s boroPro or boro(W)pro or prolin##:
3 BOROPRC
1234 BCPD
14806 PFO
7342 PROLIN##
1 BCPD(W) (PRO OR PROLIN##)
L1 3 BCPOPRO OR BORO(W) (PRO OR PROLIN##)
=> d ti,fa,date,kwic l-3

US PAT NO: 5,288,707 [IMAGE AVAILABLE] L1: 2 of 3
TITLE: Borelysine peptidomimetics
DATE FILED: Jan. 29, 1993

TITLE: Borelysine peptidomimetics
US PAT NO: 5,288,707 DATE ISSUED: Feb. 22, 1994
[IMAGE AVAILABLE]
APPL-NO: 08/011,443 DATE FILED: Jan. 29, 1993
FRN-PE. NO: 9017694 FRN FILED: Aug. 13, 1990
FRN-PE. CO: United Kingdom
FEL-US-DATA: Continuation of Ser. No. 743,847, Aug. 12, 1991,
abandoned.

SUMMARY:

PSUM(68)
BocPro=analog of proline in which the --COOH

DETDESC:

[ETD(63)

Boc-D-TMS-ol-Adgly-**boroPro**-OPin

DETDESC:

[ETD(63)

C. Boc-D-TMSal-Adgly-**boroPro**-OPin

DETDESC:

[ETP-WG

The . . . HCl, cyclizes to the boroproline derivative, which reacts then with the active ester of step B to give the unexpected Boc-D-TMSal-Adgly-**boroPro**-OPin as the major product. Flash chromatography (2:1 hexane/EtOAc) of the crude product yields the title compound (0.48 g) as a white foam, which is further purified by recrystallization from ether/hexane to give the desired product Boc-D-TMSal-Adgly-**boroPro**-OPin as a white crystalline compound.

US PAT NO: 4,935,493 [IMAGE AVAILABLE] L1: 3 of 3
TITLE: Protease inhibitors
DATE FILED: Oct. 6, 1987

DET0(21):

General . . . those skilled in the art of peptide synthesis. One exception is that in the preparation of a compound with the Pro-Thr-**boroPro** sequence. Removal of acid labile protecting groups from threonine hydroxyl group results in a complex mixture of products. Thus, the. . .

DETDESC:

DET0(22):

The . . . 5 minutes, this mixture and one equivalent of triethylamine (or other sterically hindered base) are added to a solution of H-**boroPro**-pinacol dissolved in either cold chloroform or tetrahydrofuran.

DETDESC:

DET0(23):

Preparation of boroProline-pinacol (H-**boroPro**-pinacol)

DETDESC:

DET0(36):

Preparation of Boc-Ala-Pro-**boroPro**-pinacol

DETDESC:

DET0(37):

Boc-Ala-Pro-**boroPro**-pinacol was prepared by coupling Boc-Ala-Pro-OH to H-**boroPro**-pinacol. First, the dipeptide, Boc-Ala-Pro-OBzl, was prepared by the mixed anhydride procedure. Boc-Ala-OH (10 g, 52.8 mmoles) was reacted with N-methylmorpholine. . .

DETDESC:

DET0(38):

Boc-Ala-Pro-OH (1.26 g, 4.28 mmoles) was coupled to H-**boroPro**-pinacol by the general procedure described for the preparation of Boc-Ala-Pro-OBzl. Boc-Ala-Pro-OH (1.26 g, 4.28 mmoles) was dissolved in 11 ml. . . of cold THF and triethylamine (0.597 ml, 4.28 mmoles) were added and the mixture added to a cold solution of H-**boroPro**-pinacol.HCl (1.0 g, 4.28 mmoles) in 5 ml chloroform. After dissolving the reaction product in ethyl acetate and washing with aqueous. . .

DETDESC:

DET0(4):

Preparation of H-Ala-Pro-**boroPro**-pinacol.HCL

DETDESC:

DET0(4):

1.0 g H-Ala-Pro-**boroPro**-pinacol.HCL

Preparation of Ac-Ala-Pro-**boroPro**-pinacol

DETDESC:

DETD(44)

H-Ala-Pro-**boroPro**-pinacol.HCL (0.22 g, 0.55 mmoles) was dissolved in 5 ml of THF and cooled to 0.degree. C. Acetic anhydride (0.078 ml, . . .

DETDESC:

DETD(46)

Preparation of MeOSuc-Ala-Ala-Pro-**boroPro**-pinacol.

DETDESC:

DETI(47)

MeCSuc-Ala-Ala-Pro-OH . . . procedure described in Kettner et al., J. Biol. Chem., 259: 15106-15114 (1984). MeOSuc-Ala-Ala-Pro-OH (1.59 g, 4.28 mmoles) was coupled to H-**boroPro** pinacol.HCl (1.00 g, 4.28 mmoles) by the mixed anhydride procedure described for the preparation of Boc-Ala-Pro-**boroPro**-pinacol except that, after filtration and evaporation of the reaction solvent, it was applied to a 2 cm column containing 1C. . .

DETDESC:

DETD(49)

Preparation of Boc-Pro-Thr(OBzl)-**boroPro**-pinacol.

DETDESC:

DETD(51)

Boc-Pro-Thr(OBzl)-**boroPro**-pinacol was prepared by coupling Boc-Pro-Thr(OBzl)-OH (2.70 g, 6.42 mmoles) to H-**boroPro**-pinacol.HCl(1.50 g, 6.42 mmoles) using the procedure described for Boc-Ala-Pro-**boroPro**-pinacol. The product (2.4 g) was purified by chromatography on a 2.5.times.50 cm column of LH-20 in methanol and was obtained. . .

DETDESC:

DETD(53)

Preparation of Boc-Pro-Thr-**boroPro**-Pinacol

DETD(54)

DETI(54)

Boc-Pro-Thr-**boroPro**-pinacol was prepared by hydrogenation of Boc-Pro-Thr(OBzl)-**boroPro**-pinacol (from Example 6, 0.585 g, 0.79 mmoles). The protected peptide was dissolved in 100 ml of methanol and was hydrogenated. . .

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